

Delete pages 95-97 of the Sequence Listing as submitted on February 4, 2000, and insert therefore the attached new pages 95-97.

**REMARKS**

Supplementing the amendment filed on February 4, 2000, and the supplemental amendment filed February 7, 2000, entry of the additional amendments above is respectfully requested.

Attached is a proposed set of revised Figures 7B, 7D, 7F, 7H, 7J, 7L, 7N, 7P, 7R, 7T, 7V, 7X, 7Z, and 7BB. On each of these pages as originally filed, the last two lines of sequences s1 and s5 had been erroneously omitted from the figures. These omissions have now been corrected on the attached pages. The examiner is respectfully requested to approve the revisions as marked and circled in red on the attached pages of the above figures. Once these proposed drawing corrections are approved, formal drawings can be prepared for filing after a notice of allowance is received.

The insertion of the omitted lines in the drawings and the inclusion of the corresponding sequences in the sequence listing does not comprise new matter as the two sequences of Figure 7 having portions omitted, i.e., sequence s1 and s5, are both known and previously published sequences. At page 55, lines 19-28 of the present specification as originally filed, it was

stated that Figure 7 shows the alignment of "mouse MEKK (S1)" and "SS3 (S5)". Furthermore, page 17, lines 26-29, indicate that the mouse protein kinase is "mMEKK". It is thus evident that the third "K" at page 55, line 20, was a typographical error and this has now been corrected.

The mMEKK protein sequence was disclosed in Lange-Carter et al "A Divergence in the MAP Kinase Regulatory Network Defined by MEK Kinase and Raf", Science 260:315-319 (1993). It can be seen that the sequence in Fig. 2A at page 316 is the same as that of the sequence s1 beginning at Figure 7K. Thus, the filling in of the omitted lines using the sequence of Lange-Carter is not new matter. A copy of the Lange-Carter et al publication is attached hereto.

With respect to sequence s5, page 55, line 16, indicates that this sequence was revealed by a databank search. Anyone searching the SwissProt Database using a portion of the sequence shown in Figure 7 would readily discover the existence of SwissProt p25390, a copy of which is attached hereto. It can be seen that this sequence was entered and last modified in May 1992. A comparison of this sequence with the portions of sequence s5 as shown in Figure 7 as filed will show their identity. Thus, as sequence s5 is also a sequence which was known as of the filing date of the present application, the insertion of the missing amino acid residues is merely the

correction of an obvious error which does not include the incorporation of new matter. This explanation applies not only to the correction of the drawing which is proposed herein, but also to the sequence listing which was presented with applicants' amendment of February 4, 2000, and which is being corrected herein. The sequence in the sequence listing is the same as that of the corrected drawing, and, thus, does not contain new matter for the same reasons as discussed above with respect to the corrections to the drawings.

As further proof that the corrections merely add known sequences and thus do not comprehend new matter, reference is made to Malinin et al "MAP3K-related kinase involved in NF- $\kappa$ B induction by TNF, CD95 and IL-1," Nature 385:540-544 (February 1997), which is a publication of the present invention by the present inventors. Figure 4 of this publication corresponds to Figure 7 of the present application. The correct sequence of s1 (mMEKK1) and s5 (SSC3) are shown therein. The caption to Figure 4 makes reference to the Lange-Carter publication as the source of the mMEKK1 sequence and SwissProt p25390 as the source of the SSC3 sequence.

With respect to sequence s1, it can be seen that the N-terminus of this sequence as shown in Figure 7K begins "MVTAVP", which is the sequence which starts at the line which begins at the left margin of the first line in Figure 2A of Lange-Carter.

The residue at the end of this line is numbered 75, and, therefore, as the line is 75 residues long, the "MVTAVP" at the beginning of this line begins at residue 1. However, in the previous line, there are fifteen additional amino acids which begin "MVGKL". SEQ ID NO:19 erroneously included these 15 amino acids, despite the fact that the sequence in Fig. 7 began at residue 1 of Lange-Carter ("MVTAVP..."). Accordingly, this error in SEQ ID NO:19 is being corrected herein on the attached substitute pages 95-97. SEQ ID NO:19 on the attached pages correctly begins "MVTAVP" as is shown in Fig. 7 and thus now corresponds exactly to the sequence shown in s1 in Fig. 7 as proposed to be corrected.

Furthermore, attached hereto is a 3 1/2" disk containing the "Sequence Listing" in computer readable form in accordance with 37 C.F.R. §1.821(e) which includes this amendment.

The following statement is provided to meet the requirements of 37 C.F.R. §1.825(a) and 1.825(b).

I hereby state, in accordance with 37 C.F.R. §1.825(a), that the amendments included in the substitute sheets of the sequence listing are believed to be supported in the application as filed and that the substitute sheets of the sequence listing are not believed to include new matter.

I hereby further state, in accordance with 37 C.F.R. §1.825(b), that the attached copy of the computer readable form is

the same as the paper copy of the sequence listing as filed after substitution of the attached revised pages 95-97.

Entry of the present Second Supplemental Amendment and consideration thereof in conjunction with the Amendment of February 4, 2000, and the Supplemental Amendment of February 7, 2000, are therefore earnestly solicited.

Respectfully submitted,

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